BG-12 (dimethyl fumarate)
This information sheet refers to a drug treatment that is currently not licensed in Ireland.

What is BG-12?

BG-12 (dimethyl fumarate or DMF) is an experimental oral drug for treating relapsing-remitting multiple sclerosis (RRMS). Biogen Idec (who manufactures Avonex and Tysabri) is the manufacturer.

(Of Interest: Fumaderm, a therapeutic for the treatment of psoriasis in Germany, includes dimethyl fumarate as one of the active ingredients. Fumaderm has more than 14 years of post-marketing experience and approximately 100,000 patient years of use.)

How does BG-12 work?

The mechanism of action is not fully understood. Research suggests that BG-12 may have neuro-protective and anti-inflammatory effects. It may reduce the activity and impact of inflammatory cells in the central nervous system (CNS) and bring about protective responses in CNS cells.

How is BG-12 administered?

BG-12 is taken orally as tablets, two or three times per day (once approved the recommended dosage will be known).

What are the side effects from taking BG-12?

In clinical trials, the most common side effects were; flushing and feeling hot, gastrointestinal upset, diarrhoea, nausea, abdominal pain, tiredness and headache.

No serious side effects (specific to BG-12) have been reported from clinical trials. Relapses were noted across all groups and are considered serious events.

What are the findings from BG-12 clinical trials?

In a phase II study, different doses of BG-12 were compared to placebo in people with RRMS over 24 weeks of treatment. BG-12 significantly reduced MRI-detectable brain lesion activity. A reduction in relapse rate was also observed. Following on from the success of the phase II study, two Phase III studies have been conducted, named DEFINE and CONFIRM, both having over 1,000 patients.
Results from these phase III trials were reported in 2011. The DEFINE clinical trial assessed the efficacy and safety of oral BG-12 in people with RRMS. This 2 year study compared BG-12 (240mg), taken either two or three times daily, or a placebo in more than 1200 participants with RRMS. Compared to placebo, the drug reduced the annual relapse rate by 53% for the twice daily dosing and 48% for the three times a day dosing.

BG-12 twice daily reduced the risk of disability progression by 38%, while BG-12 three times per day reduced this risk by 34%. MRI scans showed that, after two years, people receiving BG-12 had significantly fewer brain lesions compared to placebo.

The CONFIRM trial was a global, randomised, double-blind, placebo-controlled, dose-comparison study to determine the efficacy and safety of BG-12 and enrolled 1,430 people with RRMS. It was similar to DEFINE, but with an additional group who took Copaxone (glatiramer acetate/subcutaneous daily injection) for comparison. Both BG-12 and Copaxone groups were evaluated against a placebo.

At two years, BG-12 reduced annual relapse rate by 44% for the twice-daily dose and by 51% for the three times daily dose, compared to placebo. In contrast, Copaxone reduced relapse rate by 29%. BG-12, twice daily, reduced the risk of disease progression by 21% and for three times daily by 24%.

At two years, there was a significant reduction in T1 and T2 lesions in comparison to placebo. Results for the BG-12 and Copaxone treatment groups at two years compared with placebo included: BG-12 reducing the number of new or newly enlarging T2-hyperintense lesions by 71% (twice daily) and by 73% (thrice daily), while Copaxone provided a 54% reduction. BG-12 reduced new T1-hypointense lesions by 57% (twice daily) and by 65% (thrice daily) while Copaxone provided a 41% reduction.

**How does BG-12 compare to current therapies?**

In the CONFIRM clinical trial, BG-12 and Copaxone had similar outcomes, however, BG-12 performed slightly better. As it has been shown to have a good safety and tolerability record, and should be available in pill/tablet form - while Copaxone and other therapies require injections or infusions – BG-12 provides a more convenient and likely preferred method of administration, making it easier for the person with MS with self manage the treatment of their condition.

Doug Williams, Biogen's executive vice president of research and development, in an interview said “The safety profile has continued to hold up nicely from one study to the next,”. He believes BG-12 “should be front-line therapy for patients” based on the risk-benefit profile seen in BG-12 clinical trials.

**What further BG-12 studies are planned?**

We are awaiting results from EXPLORE, a phase II clinical trial, to evaluate oral BG-12 as combination therapy for patients who continue to experience disease progression despite ongoing treatment. This open-label study will evaluate the safety and tolerability of BG-12 when administered with beta interferon or glatiramer acetate to 100 people who continue to have evidence of disease activity despite receiving consistent (single) drug treatment for at least a year. The study was completed in June 2012.
In order to further assess the long-term safety and efficacy of BG-12 in RRMS, participants on the DEFINE and CONFIRM studies are taking part in a follow on study. Its estimated completion date is June 2016.

**When is BG-12 likely to become available?**

In May 2012, Biogen Idec announced that U.S. and EU regulatory authorities have accepted its marketing applications for the review of BG-12. Once it is licensed and approved, for it to be reimbursed, it must undergo a Health Technology Assessment, by the National Centre for PharmacoEconomics (NCPE) to assess if it is therapeutically beneficial and cost effective. It is hoped BG-12 will be available in early 2013.

**What does MS Ireland say in relation to BG-12?**

If approved, MS Ireland welcomes BG-12 as an additional treatment option for people with MS. The advent of new and innovative oral therapies for the treatment of MS is an important step in the management of MS as a condition. Any and all strides made by pharmaceutical companies and researchers play a crucial role in the development of better treatments to decrease the instances of relapse and limit disease progression.

**Links to further information on BG-12**

BG-12 MS Trust UK  
[http://www.mstrust.org.uk/research/drugsindevelopment/bg00012.jsp](http://www.mstrust.org.uk/research/drugsindevelopment/bg00012.jsp)

BG-12 Multiple Sclerosis Resource Centre UK  
[http://www.msrc.co.uk/index.cfm?fuseaction=show&pageid=1679](http://www.msrc.co.uk/index.cfm?fuseaction=show&pageid=1679)

Biogen's MS pill BG-12 OK'd for US/EU review  

Biogen Idec DEFINE Press Release  

Biogen Idec CONFIRM Press Release  

**Clinical Trials**

BG00012 Phase 2 Combination Study in Subjects with Multiple Sclerosis (EXPLORE)  
[http://clinicaltrials.gov/show/NCT01156311](http://clinicaltrials.gov/show/NCT01156311)

Long-Term Safety and Efficacy Study of Oral BG00012 Monotherapy in RRMS  
[http://clinicaltrials.gov/show/NCT00835770](http://clinicaltrials.gov/show/NCT00835770)

Efficacy and Safety Study of Oral BG00012 with Active Reference in RRMS (CONFIRM)  

Efficacy and Safety of Oral BG00012 in RRMS (DEFINE)  

Long-Term Safety and Efficacy Study of Oral BG00012 Monotherapy in RRMS  

**Disclaimer:**

MS Ireland provides information to the MS Community on an array of topics associated with MS. This information is for reference purposes only and medical advice should always be sought before any treatment or intervention is tried.

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